Session XI

Trophic Factors Importance for Neurodegenerative Disorders

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NEURONAL TARGETS DIRECT THEIR OWN REINNERVATION VIA CONNCENTRATION GRADIENTS OF DIFFUSIBLE FACTORS

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In vivo, diffusible factors released from denervated targets play an important role in directing the outgrowth of regenerating axons. The influence of these factors is effective over distances of many millimeters (Kuffler, 1989). The identities of the responsible molecules are unknown. *In vitro*, it has been shown that concentration gradients of neurotransmitters can direct the elongation of growth cones (Zheng et al., 1994). However, the physiological relavence of this influence remains unclear since these neurotransmitters are apparently not present where they would need to be to exert this influence. Experiments were designed to detemine whether factors released by the cells of denervated peripheral nerve tubes, which are available to regenerating axons, can direct axon growth. The cells of the peripheral nerve tube release neurotrophic factors that promote a 10 fold increase in process length of sensory neurons when compared to the process outgrowth of control neurons. We have tested whether these factors can also direct this process outgrowth. Growth cones were exposed to diffusible concentration gradients of the factors in medium conditioned by pieces of peripheral nerve, as well as the neurotransmitter acetylcholine (ACh). More than 60% of the growth cones turned and grew up the concentration gradients of ACh, while ca. 10% of the growth cones grew up the concentration gradients of the neurotrophin. While the identity of the responsible neurotrophic factor/s remains unknown, one candidate is a molecule with a molecular mass of between 30 and 100 kD, functionally related to nerve growth factor (Dobretsov, *et al.*, 1994). These results set the stage for experiments to characterize the responsible neurotropic factor and determine the mechanism by which axons "read" the chemical gradients.

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